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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
06/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,312	MAD ARIF ET AL.	
	Examiner	Art Unit	
	Nora M. Rooney	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-47* is/are pending in the application.

4a) Of the above claim(s) *18-21,25,31-39,46 and 47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-24,26-30 and 40-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed on 04/12/2007 is acknowledged.

2. Claims 18-47 are pending.

3. Claims 18-21, 25, 31-39 and 46-47 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to non-elected inventions.

4. Claims 22-24 and 26-30 and 40-45 are currently under examination as they read on the isolated nucleic acid of SEQ ID NO:1 encoding the protein of SEQ ID NO:5.

5. In view of Applicant's amendments and arguments filed on 04/12/2007, only the following rejection are maintained.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 22-24 and 26-30 and 40-45 stand rejected under 35 U.S.C. 112, first paragraph, first paragraph, because the specification, while being enabling for: the nucleic acid of SEQ ID NO:1 encoding the protein of SEQ ID NO:5 and a method of producing the protein of SEQ ID NO:5 using the nucleic acid of SEQ ID NO:1, does not reasonably provide enablement for: an

isolated nucleic acid molecule **comprising** a nucleotide sequence encoding the amino acid sequence as set forth in SEQ ID NO:5 **or conservative substitutions thereof**, wherein a protein expressed from said nucleic acid molecule is capable of inducing an allergic reaction to latex in a person sensitized to said protein in claim 22; An isolated nucleic acid molecule **comprising** a nucleotide sequence encoding a biologically active portion of the amino acid sequence as set forth in SEQ ID NO:5 **or conservative substitutions thereof**, wherein a peptide expressed from said nucleic acid molecule is capable of inducing an allergic reaction in a person sensitized to said peptide in claim 23; The nucleic acid molecule of claim 22, **comprising** the nucleotide sequence of SEQ ID NO:1 in claim 24; A vector comprising the nucleic acid molecule of claims 22-24 in claim 26. The vector of claim 26, wherein said vector is an expression vector in claim 27. An isolated host cell transfected with the vector of claim 27 in claim 28. The isolated host cell of claim 28, wherein the organism of said host cell is Escherichia coli in claim 29. A method of expressing a protein comprising the step of culturing the isolated host cell of claim 28 under conditions in which **said nucleic acid molecule** is expressed, thereby expressing **said protein** in claim 30; **A method for producing a protein in recombinant form, said method comprising the steps of: (a) inserting the nucleic acid molecule of claim 22 into an appropriate vector; and (b) inducing the vector to express said recombinant protein** in claim 40; the method of claim 40, **wherein the vector is a microorganism, a plant or an animal** in claim 41. The method of claim 41, wherein the microorganism is a bacterium, a virus or a yeast in claim 42. The method of claim 42, wherein the bacterium is Escherichia coli in claim 43. The method of claim 40, wherein, in step (b), said vector is exposed to an inducer in

claim 44; and the method of claim 44, wherein said inducer is isopropyl thiogalactoside (IPTG) in claim 45 for the same reasons as set forth in the Office Action mailed on 01/12/2007.

Applicant's arguments filed on 04/12/2007 have been fully considered, but are not found persuasive.

Applicant argues that it would not require an undue amount of experimentation to determine which nucleic acids, vectors and host cells can be used in the claimed invention. Applicant argues that conservative substitutions to the protein of SEQ ID NO:5 would be "well understood in the art and entirely predictable...with a high probability of retaining biological activity." (In particular, second paragraph, page 8 of the response filed on 04/12/2007). Applicant argues that the uncertainly in the substitutions and additional amino acids added onto the N- and/or C- terminus of SEQ ID NO:5 is removed by the recitation of the requirement for retention of allergen activity.

The Examiner argues that there is tremendous variability in the importance of individual amino acids in protein sequences. Since the amino acid sequence of SEQ ID NO:5 is a key determinant of allergenic activity, single residue substitutions can have severe phenotypic effects. There is no simple way to infer the likely effect of an amino acid substitution on the basis of sequence information alone. For example, Burgess et al (PTO-892, Reference U; In particular, whole document) teaches that a conservative replacement of a single "lysine" reside at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial loss of

heparin binding, receptor binding and biological activity of the protein. Similarly, Lazar et al. (PTO-892, Reference V; In particular, whole document) teaches that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagines did not affect biological activity, while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. Wang et al. (PTO-892, Reference W) also teaches that single amino acid differences can result in drastically altered functions between two proteins. A single amino acid determines lysophospholipid specificity of the S1P1 (EDG1) and LPA1 (EDG2) phospholipids growth factor receptors because Glu^{121} in the Arg-Glu-Gly motif of S1P1/EDG1, which corresponds to Gln^{125} in the Arg-Gln-Gly motif of LPA1/EDG2, leads to a ligand selectivity switch in concert with the mutations by influencing the specificity for S1P or LAP (In particular, abstract, page 49213, last paragraph). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Furthermore, the specification fails to teach what substitutions and mutations of SEQ ID NO:5 can be tolerated that will allow the protein to function as claimed with retained allergenic activity. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with reasonable expectation of success are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or no substitutions. Residues that are directly involved in protein functions such as binding will certainly be among the most conserved (PTO-892, Reference X; In particular, page 1306, column 2). Thus, it would require an undue amount of experimentation by the skilled

artisan to determine which sequences of SEQ ID NO:5 would have the function of the full length molecule and, in turn, to identify nucleic acid sequences other than SEQ ID NO:1 which encode these sequences.

Further, the specification does not disclose support for the limitation of claim 41 wherein the vector is a microorganism, plant or animal. Vectors for use in the claimed invention are not microorganisms, plants or animals, but rather they are derived from or put into host cells from microorganisms, plants or animals.

The method recited in Claim 40 is not adequately disclosed in the specification because the recited method will not produce protein. The recited vector must be present in a host cell system in order to produce protein. Therefore, it is unclear how one of ordinary skill in the art would be able to practice the invention without undue experimentation.

8. No claim is allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

May 31, 2007

Nora M. Rooney, M.S., J.D.

Patent Examiner

Maher M. Haddad

MAHER M. HADDAD
PRIMARY EXAMINER